IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	WEINER et al.	
Serial No.:	08/061,699	Group: 1806
Filed:	May 12, 1993	Examiner: Schwadron, R.
Title:	CONSERVED MOTIF OF HEPATITIS C VIRUS E2/NS1 REGION	Atty. Docket No: 0938.001

DECLARATION UNDER 37 CFR § 1.132

I, Amy Weiner, declare as follows:

1. I am presently a Senior Scientist in the area of Non-A, Non-B Hepatitis research at Chiron Corporation in Emeryville, California. A copy of my curriculum vitae, describing my background and qualifications, is attached to this Declaration as Exhibit A.

2. During the last twelve (12) years I have conducted research in viral hepatitis at Chiron Corporation. During this time I have been directly involved in the research supporting HCV diagnostics and vaccine development and I am a co-inventor of the above-referenced patent application.

3. In addition to working directly in research supporting HCV diagnostics and vaccine development, I have also been directly involved with the preparation and use of antibodies raised against recombinant HCV immunogens, including the immunogens of the above-referenced patent application having a conserved amino acid motif in the E2/NS1 hypervariable region of the HCV genome, for dectection of and passive immunization against HCV. I also have knowledge of the currently available and art-recognized models, or living systems, in which the anticipated therapeutic utility of newly discovered antibodies can be assessed. In particular, I have direct knowledge of the use of the chimpanzee animal system in Example 3 of the above-referenced application, and of the protocol for passive immunization and qualitative assessment used therein.

4. The subject application encompasses the outcome of research and development efforts that were directed ,in part, to the development of anti-HCV antibodies for use in the prevention, treatment and detection of HCV infection in humans.

5. Based on the following factual considerations, I believe, as one having skill in the art, that the protective effect of the passive immunization of the chimpanzee of Example 3 reasonably correlates to, or alternatively, is reasonably predictive of the asserted utility in human subjects. Additionally, the antibodies raised for Example 3 correspond to the scope of the antibodies claimed, for example, in claim 13 of the application.

(a) Experimental work with HCV is encumbered by the paucity of animal models for what is essentially a virus specific for higher primates. The chimpanzee is the only *reliable* model recognized in

the field. Moreover, the chimpanzee is a higher primate. A copy of a publication to Choo et al., entitled "Vaccination of chimpanzees against infection by the hepatitis C vaccine," *Proc. Natl. Acad. Sci., USA*, Vol. 91, pp 1294 - 1298 (Feb. 1994) is attached hereto as Exhibit B and demostrates that the chimpanzee test subject has continued acceptability for reliability by those having skill in this field.

(b) The effect of passive immunization of the chimp of Example 3 was measured qualitatively by PCR assay for HCV RNA, electron microscopic observation of liver biopsy specimens, and ELISA assay, and was found to be very effective. It is well-known that inoculation of chimpanzees with HCV leads to infection of the liver, and is associated with abnormal liver function tests and abnormal liver histology. Also, the required dose for infection in chimpanzees is well-established to those of ordinary skill, and concommitant viral replication is inevitable.

The inoculation of the chimp in Example 3 was 10 times the dose required to confer an infection to an unprotected chimpanzee. Highly sensitive PCR assay after challenge did not detect any signs of viral replication, indicating that complete protection had been conferred by the passively administered antibodies.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 3/15/96

Dr. Amy J. Weiner